REMARKS

Claims 31 to 39 and 41 to 61 are pending in the application; claim 40 is canceled.

Election/Restriction

Applicant had pointed out in the response to the election/restriction requirement that *Policastro et al.* does not teach the sequence between 371 and 393 that is identical to SEQ ID NO. 3. The reference cited in the previous office action (page 2, paragraph 2) dated 4/26/07 is (see also PTO-892 attached to this office action) is:

Policastro et al. (1983) J.of Biol Chem. Vol, 258; No. 19, PP 11492-11499

The reference the examiner cites in the office action dated 6/25/07 is:

Policastro et al. (1986) J. Biol. Chem. 261 (13), PP 5907-5916

The examiner has cited an entirely different reference in the initial restriction requirement and this first reference fails to show the SEQ ID NO. 3. Applicant has made an election based on false information provided by the examiner and objects to such careless citations made by the examiner.

As regards the disclosure of SEQ ID NO. 3 within a region of a chromosome in the newly cited reference, it is respectfully submitted that according to the *Trilateral Project 24.1* of the JPO, EPO and USPTO, *Biotechnology Comparative Study on Biotechnology Patent Practices Comparative Study* (copy attached), page 18, 2nd to last paragraph, it is generally accepted practice in all Patent Offices that a partial sequence or fragment is **novel** when an invention relating to a partial sequence has not been disclosed in concrete terms in publicly known literature.

Therefore, even though the cited reference discloses a sequence of which SEQ ID NO. 3 is a section, the SEQ ID NO. 3 itself is still novel as the particular sequence and its use/application has not been disclosed in the prior art.

Therefore, SEQ ID NO. 3 is considered novel and a technical feature defining the invention over the prior art

Reconsideration is respectfully requested.

Claim Objections

Claim 40 is objected to; claim 40 has been canceled.

Claim Rejections - 35 U.S.C. 112

Claims 31 and 40-42 stand rejected under 35 U.S.C. 112, 2nd paragraph, as being indefinite as regards the step which relates back to the preamble.

Claim 31 has been amended to include in step b) a feature according to which the detection of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG indicates receptivity of the endometrium for implantation. Thus, the claim language now provides proper relation between the preamble and the method steps in that the receptivity of the endometrium is defined as the result.

Claims 41 and 42 define specifics as regards the determination of the receptivity.

Reconsideration and withdrawal of the rejection of the claims under 35 USC 112 are therefore respectfully requested.

Claims 40-42 are rejected under 35 USC 112, second paragraph as omitting an essential step.

The amendment to claim 31 has provided an essential step for determination of receptivity so that the omission in the dependent claims is cured as well.

Reconsideration and withdrawal of the rejection of the claims under 35 USC 112 are respectfully requested.

Rejection under 35 U.S.C. 102

Claims 31 and 40 stand rejected under 35 U.S.C. 102(b) as being anticipated by *Bellet et al. (US 6,194,154)*.

Claim 31 has been amended to specify that in the blood sample or tissue sample the expression or over expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG is measured quantitatively and that the detection of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG indicates receptivity of the endometrium for implantation.

Thus, a method is provided that enables determination of whether or not the endometrium is receptive for implantation simply by measuring the expression or over expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG. When no expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG is detected, the endometrium is not receptive. When expression of mRNA of at least one of β7-hCG, β6-hCG, and β6e-hCG is detected, the endometrium is receptive. This is set forth in the

specification, for example, in the paragraph bridging pages 11-12; 4th paragraph of page 12; the paragraph bridging pages 12-13; and lines 15-16 of page 13.

Bellet et al. discloses a method for determining the malignant transformation of human cells that compares the over expression of hCG β3, β5, β8, and β9-mRNA in malignant mammalian, bladder, thyroid, prostate and colon cells (see Table 3 in col. 8) with the expression of hCG β7, β6 in non-malignant (normal) cells of the respective organs. An increase of the mRNA expression of hCG β3, β5, β8, and β9 in relation to the total β gene expression in the malignant cells may be determined. It is well known that hCG β3, β5, β8, and β9 are embryonic genes that are not expressed in normal tissue but are switched on again in malignant tumors. In normal tissue of the afore mentioned organs hCG β7, β6 is expressed and the expression of hCG β3, β5, β8, and β9-mRNA is an indicator for cancerous growth (see col. 2, lines 26-30). Therefore, hCG β7, β6 represent simply a standard or control. It is therefore impossible to derive based on the cited reference any teaching in regard to the importance of hCG β7, β6 as a means for determining the receptivity of the endometrium.

The cited reference does not relate at all to the endometrium or to determining the receptivity of the endometrium. The reference discloses that in "normal" tissue hCG β7, β6 are expressed. This applies to the organs mentioned in the reference, i.e., mamma, bladder, thyroid, prostate and colon. However, as found by the instant inventors, the endometrium does not express hCG β7, β6 unless the endometrium is receptive (page 13, lines 15-16, of the instant specification).

The prior art reference therefore provides no teaching at all in regard to the expression of hCG β7, β6 in the endometrium and particularly provides no teaching in regard to determining the receptivity of the endometrium.

Claim 31 is therefore not anticipated or obvious in view of the cited reference.

Rejection under 35 U.S.C. 103

Claims 41 and 42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Bellet et al. (US 6,194,154)* and *Acosta et al.*

Bellet et al. has been discussed supra and reference is being had to that discussion.

Acosta et al. is directed to endometrial dating and determination of the window of implantation in fertile women. The procedure attempts to find the best point in time for implantation. In contrast, the present invention aims at determining whether the endometrium is healthy and is capable of implanting a fertilized egg.

More importantly *Acosta et al.* does not relate to and does not use assaying of β7-hCG, β6-hCG, and β6e-hCG. *Acosta et al.* employs integrins and other molecules such as LID IL-IR, MAG etc. for determining the window of implantation.

Neither *Bellet et al.* nor *Acosta et al.* nor their combined teaching can provide a suggestion that the expression of hCG β7, β6 in a blood sample or a tissue sample can be an indicator of receptivity of the endometrium.

Moreover, the method of *Acosta et al.* requires biopsies of the endometrium in the uterus (see page 790, bottom of right column, heading "Endometrial Biopsies"); contrary to examiner's assertion there is no disclosure that a mucous membrane sample can be taken from the cervix. Also, blood samples were taken only to monitor the endocrine normality (see page 790, right column, under the heading "Volunteers").

The endometrial biopsies according to *Acosta et al.* are taken from the uterine fundus which is the end remote from the cervix. A biopsy is an invasive procedure and damages the tissue. In contrast, the present invention simply employs a cotton swab (see page 13, 1st full paragraph) or something similar to take a sample from the cervix; this is a gentle, non-invasive procedure that can be done easily and requires no particular preparation.

In regard to claim 42, it is respectively submitted that endometrial cells can be found in the menstrual blood - this is known in the art. However, the inventors have found that the endometrial cells express β7, β6 and β6e hCG and that the expression of β7, β6 and β6e hCG indicates the receptivity of the endometrium. The inventors have thus developed a method according to which menstrual blood can be used to determine the receptivity of the endometrium; this is novel and not obvious in view of the cited art.

Thus, claims 41 and 42 are not obvious in view of the cited references.

Reconsideration and withdrawal of the rejection of the claims 41 and 42 under 35 USC 103 are therefore respectfully requested.

CONCLUSION

In view of the foregoing, it is submitted that this application is now in condition for allowance and such allowance is respectfully solicited.

Should the Examiner have any further objections or suggestions, the undersigned would appreciate a phone call or **e-mail** from the examiner to discuss appropriate amendments to place the application into condition for allowance.

Authorization is herewith given to charge any fees or any shortages in any fees required during prosecution of this application and not paid by other means to Patent and Trademark Office deposit account 50-1199.

Respectfully submitted on October 25, 2007.

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